201-14526

CYTEC

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May 30, 2003

U.S. Environmental Protection Agency
Chemical Right-To-Know Program
PO Box 1473
Merrifield, VA 22116
ATTN: Mr. Richard Hefter

Dear Mr. Hefter:

In keeping with Cytec's 1999 commitment to the EPA High Production Volume Voluntary program, attached find a robust summary and test plan for 6-tert-butyl-3-(chloromethyl)-2,4-xylenol (CAS # 23500-79-0).

The robust summary and test plan is provided as hard copy and in pdf format.

Sincerely,

Randy Deskin, Ph.D., DABT
Director, Toxicology and Product Regulatory Compliance Department

TEST PLAN FOR 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol (CAS NO. 23500-79-0)

OVERVIEW

Cytec Industries Inc. agrees to sponsor 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol (CAS No. 23500-79-0) in the U.S. EPA High Production Volume Chemical Program. The sponsor hereby submits a test plan for this substance. It is our intent to use existing data plus modeling data, and additional testing as proposed in the test plan to fulfill the Screening Information Set (SIDS) endpoints.

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Table 1. Test Plan Matrix for 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol (CAS No. 23500-79-0)

CAS No. 23500-79-0	Information	Estimation	Acceptable	New Testing Required
ENDPOINT	Y/N	Y/N	Y/N	Y/N
PHYS/CHEM PROPERTIES				
Melting Point	Y	N	Y	N
Boiling Point	Y	Y	Y	N
Density (NR)	Y	N	Y	N
Vapor Pressure	Y	N	N	Y
Partition Coefficient	Y	Y	Y	N
Water Solubility	Y	Y	N	Y
ENVIRONMENTAL FATE				
Photodegradation	Y	Y	Y	N
Stability in Water	N	N	N	N
Biodegradation	N	N	N	Y
Transport between Environmental Compartments (Fugacity)	Y	Y	Y	N
ECOTOXICITY				
Acute Toxicity to Fish	Y	Y	N	Y
Acute Toxicity to Aquatic Invertebrates	Y	Y	N	Y
Toxicity to Aquatic Plants	Y	Y	N	Y
TOXICOLOGICAL DATA				
Acute Toxicity	Y	N	Y	N
Repeated Dose Toxicity	N	N	N	Y
Genetic Toxicity-Mutation	Y	N	Y	N
Genetic Toxicity-Chromosomal Aberrations	N	N	N	Y
Toxicity to Reproduction (NR)	N	N	N	N
Developmental Toxicity	N	N	N	Y
OTHER TOXICITY DATA				
Skin Irritation (NR)	Y	N	Y	N
Eye Irritation (NR)	Y	N	Y	N

Y = yes; N = no; NR = not required

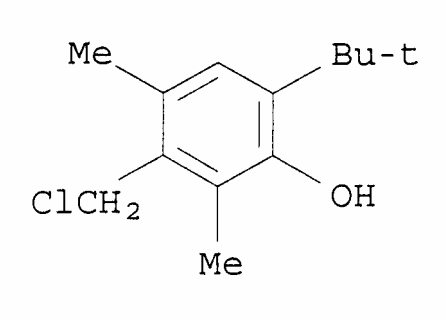
TABLE OF CONTENTS

1. Introduction

Cytec Industries Inc. has agreed to supply hazard and exposure information under The U.S. EPA High Production Volume Chemical Program for 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol (CAS No. 23500-79-0). This plan identifies existing data of adequate quality for this chemical, and outlines the intended testing to be conducted.

2. Designation of Test Substance

The test substance presented in this test plan is 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol (CAS No. 23500-79-0). Its chemical structure is as follows:



This substance has the following synonyms:

2,4-dimethyl-3-(chloromethyl)-6-tert-butylphenol
3-(chloromethyl)-6-(1,1-dimethylethyl)-2,4-dimethylphenol
4-tert-butyl-3-hydroxy-2,6-dimethylbenzyl chloride
6-tert-butyl-2,4-dimethyl-3-chloromethyl phenol
6-tert-butyl-3-chloromethyl-2,4-dimethylphenol
phenol, 3-(chloromethyl)-6-(1,1-dimethylethyl)-2,4-dimethyl-
phenol, 6-tert-butyl-3-chloromethyl-2,4-xylenol

The trade name of 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol is A-1846. From this point forward, the material will be referred to by this acronym.

According to a MSDS sheet supplied by Cytec Industries Inc., A-1846 is usually stored with 11-13 wt. % methyl isobutyl ketone (CAS No. 108-10-1) added to liquefy the product. The product is also expected to contain 2-4 wt. % of 6-tert-butyl-2,4-xylenol.

3. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate.

4. Discussion of Available Test Information

The A-1846 test plan matrix (as shown in Table 1 on page 2) was constructed after a careful evaluation of all existing data (see below). This matrix is arranged by study type (columns) and screening data endpoints (rows), and indicates if data are provided for each end point in the sets of robust summaries.

4.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

Table 2. Chemical/physical properties of A-1846

Endpoint	A-1846 (CAS No. 23500-79-0)
Molecular weight grams/mol	226.75
Melting point	45 ºC [a,c] -32 ºC [a,d]
Boiling point	ca. 320 ºC [b,c] 156 ºC [a,d]
Relative density	1.044 g/cm^3 [a,d]
Vapor pressure (hPa at 20-25° C)	0.00018 [b,c] 12 [a,d]
Partition coefficient (Log Pow or Kow)	5.32 [b,c] 3.9 [a,d]
Water solubility (mg/l at 25 ° C)	10.19 [b,c] 500[d]

[a] Measured value; [b] Estimated using EPIWIN; [c] neat material; [d] industrial product liquefied with 11-13% methyl isobutyl ketone

4.1.1 Melting Point

A melting point of 45 ºC for the neat material is reported by the Cytec Industries Inc. (personal communication from internal documents). A melting point of -32 ºC is reported for the material in 11-13% methyl isobutyl ketone (Cytec Industries Inc. 2000).

4.1.2 Boiling Point

EPIWIN Mpbpwin was used to estimate a boiling point of about 320 ºC based on the structure of the molecule and a measured melting point of 45ºC. The substance is manufactured and stored as a liquid diluted with methyl isobutyl ketone. Therefore this material has a boiling point (156ºC) more reflective of that of methyl isobutyl ketone (115.8ºC). This boiling point information is deemed adequate for this substance, which in the pure state is not expected to boil below 250ºC and may, in fact, tend to decompose before boiling.

4.1.3 Vapor Pressure

The substance is isolated and used as a liquid with 11-13% methyl isobutyl ketone solvent present. The vapor pressure of this material is close to that of methyl isobutyl ketone (12 hPa at 20ºC). The vapor pressure estimated by EPIWIN Mpbpwin for the neat material is 0.00018 hPa. No measured vapor pressure data are available for the neat substance. Therefore, vapor pressure testing is proposed (OECD Test Guideline 104) for the neat material to assist in any determination of potential for release to the atmosphere.

4.1.4 Octanol/Water Partition Coefficient

EPIWIN Kowwin has been used to estimate a log Kow of 5.32. This highly positive value is consistent with the aromatic, non-polar molecular structure. The log Kow value reported for A-1846 in 11-13% methyl isobutyl ketone is 3.9

4.1.5 Water Solubility

EPWIN Wskow (v1.40) estimates a water solubility of 10.19 mg/l at 25 ºC, and the water solubility of 1846 in 11-13% methyl isobutyl ketone is 500 mg/l. Since there are no measured water solubility values for the neat substance, testing for water solubility is proposed (OECD Test Guideline 105).

4.1.6 Summary/Test Plan for Physical Properties

Testing is planned to obtained measured values for vapor pressure and water solubility of the neat material. The data obtained from these studies will be useful to better predict environmental fate for the substance.

4.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 3.

4.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/Aop (v1.90). An overall hydroxyl radical rate constant of 14.3539 E-12 cm^3/(molecule*sec) was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 8.942 hours was calculated assuming a constant concentration of OH radical and pseudo first order kinetics.

4.2.2 Stability in Water

EPIWIN Hydrowin cannot derive a water hydrolysis rate constant for this substance. Since the substance does not contain functional groups that are known to be readily hydrolyzed, such as ester groups, nitriles, amides, etc., this substance is not expected to hydrolyze readily under

Table 3. Environmental fate parameters for A-1846

Endpoint	Value
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)[a] (Atmospheric $T_{1/2}$) [a]	 14.3539 E-12 cm^3/molecule-sec 8.942 hours
Stability in Water [a]	Not expected to hydrolyze appreciably
Henry's Law Constant[a]	6.85E-007 atm-m^3/mol
Koc[a]	1.705E+4
Bioconcentration Factor (log BCF) [a]	2.945
Environmental transport (Fugacity Level III mass percentages)[a]	Air = .0002 Water = 11.6 Soil = 47.6 Sediment = 40.8
Biodegradation [a]	One linear Model – readily biodegradable Others- not readily biodegradable

[a] Estimated using EPIWIN

neutral, ambient conditions. In addition, the very limited water solubility of this substance further reduces the potential for hydrolysis.

4.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using the EPIWIN model. Inputs to the program are CAS No. 23500-79-0 and a melting point of 45 ºC. Emission rates inputted into the program were air: 0 kg/hr, water: 1000 kg/hr, soil: 1000 kg/hr and sediment: 0 kg/hour. The following half-lives were calculated: T ½ air = 17.88 hrs, water = 1440 hr, soil = 1440 hr, and sediment = 5760 hr. The Biowin ultimate estimate is in the range of months. A Henry's Law Constant of 6.85E-7 atm-m^3/mol and a soil sediment partition constant (Koc) of 1.705E+4 were estimated using the EPIWIN/Henry and Pckoc Programs, respectively. The percent mass balances predicted for thiodipropionitrile in air, water, soil and sediment are shown in Table 3.

4.2.4 Biodegradation

A study that provides data on the rate and extent of biodegradation of A-1846 in the aqueous environment is not available. Results of the majority of the models used in the EPWIN suite indicate that the material biodegrades slowly; however, one model indicates that the material biodegrades fast. Since this modeling is not consistent, it is not sufficient to fill this endpoint. Biodegradation testing is therefore proposed (OECD Test Guideline 301 B or D).

4.2.5 Bioconcentration

A bioconcentration factor was calculated using the EPIWIN BCF Program (log BCF = 2.945). This value indicates that the material has some potential to bioaccumulate.

4.2.6 Summary/Test Plan for Environmental Fate Parameters

Estimated values are available for the hydroxyl radical induced photolysis rate constant and atmospheric half-life, Henry's Law Constant, soil sediment partition coefficient, Fugacity Level III environmental transport parameters and bioconcentration factor. No further testing is planned for these endpoints. No testing is planned for water stability (hydrolysis) because this material does not have functional groups known to be easily hydrolyzed under neutral ambient conditions, and because this substance has very limited solubility in water. Biodegradation testing is planned, since the results of EPIWIN modeling are not consistent.

4.3 Ecotoxicity

4.3.1 Acute Toxicity to Fish

The 96-hr LC50 value for fish estimated by the EPA's ECOSAR model for the phenol class is 0.300 mg/l, and for the benzyl halide class is 0.118 mg/l. No measured data are available, therefore testing is proposed.

4.3.2 Acute Toxicity to Aquatic Invertebrates

The EPA's ECOSAR models for phenols or benzyl halides predict 48-hour EC50 values of 0.535 and 0.118 mg/l for Daphnia, respectively. No measured data are available, therefore testing is proposed.

4.3.3 Acute Toxicity to Aquatic Plants

The 96-hr EC50 values calculated for green algae by the ECOSAR models for phenols or benzyl halides are 0.130 and 0.118 mg/l, respectively. No measured data are available, therefore testing is proposed.

4.3.4 Summary/Test Plan for Ecotoxicity

LC50 and EC50 toxicity values have been estimated by EPIWIN ECOSAR for fish, Daphnia and green algae. No aquatic toxicity studies are currently available that provide reliable measured data. Therefore the sponsors propose to conduct new aquatic acute studies in fish, daphnia and algae (OECD Test Guidelines 201, 202, and 203).

4.4 Human Health Data

4.4.1 Acute Mammalian Toxicity

This endpoint is filled by sufficient oral, inhalation and dermal toxicity studies in rodents. The LD_{50} value for the oral study in male rats conducted with A-1846 of 80.5 % purity is 7.71 ml/kg, or 8.04 g/kg (Brown, 1979). Results of an OECD Guideline 423 study indicate that the oral LD50 value for a more pure material in male and female rats is > 2000 mg/kg (Driscoll, 2000). According to a material safety data sheet, the 4-hour LC50 value for inhalation in the rat is > 2000 ppm (8.36 mg/l)(Cytec Industries Inc., 2000). The dermal LD_{50} value in rabbits was 9.98 ml/kg, or 10.4 g/kg (Brown, 1979).

Signs of toxicity in rats orally exposed to 2000 mg/kg purified test material were hunched posture, diarrhea, lethargy and pilo-erection (Driscoll, 2000). Animals recovered 2-4 days after dosing, and no abnormalities were found at necropsy. In a different study, all animals exposed to 5 or 10 ml/kg unpurified test material had a sluggish, unsteady gait after 1 hour of treatment (Brown, 1979). All animals treated with 5.0 ml/kg and 1/5 treated with 10.0 ml/kg recovered within 2 days. Four out of five treated with 10.0 ml/kg died. Animals that died exhibited distended, gas-filled and injected stomachs, with glandular portions mottled pink and yellow; red kidney medullae; distended, liquid, blood-filled and injected intestines that were yellow and red in areas; and red adrenals. Survivors of this study exhibited stomachs adhered to abdominal walls and livers at necropsy.

In rabbits treated dermally with up to 10.0 ml/kg A-1846, no clinical signs of systemic toxicity were noted. However, erythema, edema, ecchymosis, areas of necrosis, and scabs were noted at the test site in several animals over the course of the study. One out of 4 rabbits treated with 3.2 ml/kg and 2/4 treated with 10.0 ml/kg died. These animals exhibited red kidneys at necropsy. Surviving animals in all groups treated with 3.2 to 10.0 ml/kg lost weight over the course of the study. Gross necropsies of these animals were normal.

4.4.2 Repeated Dose Mammalian Toxicity

No repeated dose toxicity experiments have been performed with A-1846. As documented in Appendix 1[1], A-1846 qualifies as a "type a" site limited, closed system, industrial intermediate. As this is a site-limited, isolated intermediate, we propose to conduct a 28-day repeat dose oral toxicity study (OECD Test Guideline 407).

4.4.3 Genetic Toxicity

4.4.3.1 Mutagenicity

An OECD Guideline 471 test with 15 to 5000 micrograms/plate purified A-1846 has been performed on 4 strains of *S. typhimurium* (TA98, TA100, TA1535 and TA1537) and *E. coli* strain WP2uvrA- (Thompson, 2000). Results of this study and an additional screen performed with 1000 micrograms/plate in the same strains (Caterson, 1978) were negative. The OECD study is considered adequate to fill the endpoint. No additional testing is necessary.

[1] Detailed documentation of the information required to substantiate manufacture and use as an industrial intermediate with limited exposure is provided in Appendix I of this test plan.

4.4.3.2 Chromosomal aberration

No tests for this endpoint were located. In vitro testing is proposed for this endpoint (OECD Test Guideline 473).

4.4.4 Reproductive and Developmental Toxicity

Reproductive or developmental toxicity tests with A-1846 have not been conducted. Since the potential for significant human exposure is strictly limited, it is believed that this material qualifies for exemption from reproductive toxicity testing. We propose to conduct a developmental toxicity assessment (OECD Test Guideline 414).

4.4.5 Additional Data

4.4.5.1 Skin Irritation

The results of a dermal toxicity study in rabbits with material of 80.5% purity indicate that A-1846 is irritating to skin (Brown, 1979).

4.4.5.2 Eye Irritation

The commercially stored material that contains 11-13% methyl isobutyl ketone is severely irritating to rabbit eyes (Brown, 1979). Tissue destruction or an irreversible change in tissue occurred within 24 hours of instillation of 0.1 ml test material. The effect of washing was not assessed.

4.4.6 Summary/Test Plan for Mammalian Toxicity

Adequate acute toxicity studies have been conducted for A-1846. Results of these studies show that exposure to fairly large amounts of A-1846 is required to produce acute toxicity. The material is irritating to the skin and eyes, and is not mutagenic.

Since a chromosomal aberration test has not been performed, testing for this endpoint is proposed (OECD Test Guideline 473). Reproductive/developmental toxicity testing has not been performed. Since the material is used exclusively as an intermediate, reproductive testing should not be required. A 28-day repeat dose toxicity test (OECD Test Guideline 407) will be conducted to further characterize the toxicity of the material. In addition, we propose to conduct a developmental toxicity assessment (OECD Test Guideline 414).

5. Summary

<u>Physical properties</u>
Adequate data are available for melting point and partition coefficient. A boiling point determination is not needed, because this material is not isolated as the neat substance, and because the EPIWIN Mpbpwin estimate of 320ºC is consistent with a very high boiling point that is consistent with the molecular structure of this substance. For the neat material, measured data

are missing for vapor pressure and water solubility. Therefore, testing is planned for these endpoints.

Environmental fate properties
EPIWIN modeling provides adequate data for partition coefficient, hydroxyl radical-induced atmospheric photodegradation and environmental transport, as well as bioconcentration factor and Henry's Law Constant. No testing is planned for water stability (hydrolysis) because this material does not have functional groups known to be easily hydrolyzed under neutral ambient conditions, and the predicted water solubility for the material is low. Since no measured data are available regarding biodegradation, testing for this endpoint is planned, even though the potential for environmental release of significant quantities of this closed system industrial intermediate is limited.

Aquatic toxicity
Testing in fish, Daphnia or algae has not been performed. The LC/EC_{50} values for A-1846 in these species estimated using EPIWIN are fairly low. Therefore, acute aquatic testing is proposed for fish, daphnia and algae.

Mammalian toxicity
Adequate acute mammalian toxicity and mutagenicity data are available, and no testing is proposed for these endpoints. No repeat dose, chromosomal aberration or developmental toxicity studies are available and testing is planned for these endpoints. No reproductive toxicity data are available, but because A-1846 is manufactured and used exclusively as a site limited, closed system industrial intermediate (See Appendix 1 for further documentation), testing is not required or planned for this endpoint.

6. References

Brown DR. 1979. Antioxidant A-1846 Range Finding Toxicity Tests: Single Oral Dose, Single Dermal Dose, Skin Irritation, Eye Irritation. Carnegie-Mellon University Institute of Research, Report No 42-556, for American Cyanamid Company, dated July 26.

Caterson C. 1978. Mutagenicity test report (Ames Salmonella test) for A-1846. Report Number M78-170 from CRD Division, Plastics Additives Department, American Cyanamid.

Cytec Industries Inc. 2000. Material safety data sheet for A-1846, dated 10/30/200.

Driscoll R. 2000. Purified A-1846 (CT-684-00). Acute oral toxicity in the rat - acute toxic class method. SafePharm Laboratories Limited Project Number 971/115 for Cytec Industries, Inc., dated October 3.

EPIWIN AOP (v1.90).

EPIWIN BCF (v2.14).

EPIWIN ECOSAR (v0.99g).

EPIWIN HENRY (v3.10).

EPIWIN HYDROWIN (v1.67).

EPIWIN KOWWIN (v1.66).

EPIWIN Level III Fugacity modeling program.

EPIWIN MPBPWIN (v1.40).

EPIWIN PCKOC Program (v1.66).

EPIWIN WSKOW (v1.40).

Klimisch HJ, Andreae M and Tillmann U. 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Reg Tox Pharm 25:1-5.

Thompson PW. 2000. Purified A-1846 (CT-684-00). Reverse mutation assay "Ames Test" using Salmonella Typhimurium and Escherichia Coli. SafePharm Laboratories Limited Project Number 971/116 for Cytec Industries Inc., dated October 30.

APPENDIX I

Documentation of manufacture and use of 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol (CAS No. 23500-79-0) as a site-limited, closed system industrial intermediate

According to the EPA "Guidance for Testing Closed System Intermediates for the HPV Challenge Program,"any chemical which is intended to undergo a further deliberate reaction to produce another industrial substance is considered an intermediate."
It is believed that 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol fits the description of a type (a) closed system industrial intermediate. This description is as follows:

a) isolated intermediates which are stored in controlled on-site facilities

The EPA guidance also states that documentation is to be provided to support the claim for reduced testing. Such documentation includes information on number of sites, basis for closed process, and information on release, transportation or presence in distributed product. This information for 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol is provided below:

6-tert-Butyl-3-(chloromethyl)-2,4-xylenol is manufactured and converted at one plant site in the United States. This site is owned and operated by Cytec Industries Inc. Manufacture is carried out in a closed system (stainless steel reactor) by the chloromethylation of 6-tertiarybutyl-2,4-dimethylphenol using paraformaldehyde and hydrochloric acid (HCl). Some bis-chloromethyl ether (BCME) is formed as a byproduct from HCl and formaldehyde. BCME is a carcinogen regulated by the Occupational Safety and Health Administration (OSHA) (29 CFR 1910.1003), and these regulations apply to any area in which bis-chloromethylether may be processed or handled in concentrations greater than 0.1% by weight or volume in solid or liquid mixtures. These regulations require the use of a regulated area with access restricted to authorized employees only. Manufacture is carried out by remote control in a closed system operation within the required regulated area. If authorized employees must enter the regulated area for sampling when BCME may be present in the process at concentrations greater than 0.1% by weight or volume, they must wear a Saranek Tyvek suit, a self-contained breathing apparatus, impervious gloves, and boots. Then prior to each exit from the regulated area, the authorized employee must remove and leave protective clothing and equipment at the point of exit. At the last exit of the day, the authorized employee must decontaminate their personal protective equipment using water by standing under the Safety shower, then immediately upon exiting, the authorized employee must place their Saranek Tyvek suit and gloves into a properly labeled waste drum. While operated as a regulated area, the environment is kept under negative pressure with respect to non-regulated areas. Off-gases from the reactor are vented through a caustic scrubber to destroy residual BCME.

Following reaction, the aqueous layer is separated for recycle to the next batch. The organic layer containing the product 6-tert-butyl-3 (chloromethyl)-2,4-xylenol is washed with salt water to remove traces of residual HCl and formaldehyde from the product and to hydrolyze any traces

of residual BCME. The saltwater wash layers are sent to the plant wastewater treatment system. The product is dehydrated under vacuum to remove residual water, and is then diluted with 11-13 % (wt. %) methyl isobutyl ketone (MIBK) and transferred through a closed line to a closed storage tank. The stringent controls applied to prevent exposure to BCME also prevent exposure to 6-tert-Butyl-3-(chloromethyl)-2,4-xylenol during manufacture.

6-tert-Butyl-3-(chloromethyl)-2,4-xylenol in MIBK is transferred from its storage tank via a closed line to another closed reactor, where it is chemically converted on site to a commercial antioxidant. This is the only use of 6-tert-butyl-3-(chloromethyl)-2,4-xylenol, with none of the 6-tert-butyl-3-(chloromethyl)-2,4-xylenol being sold, formulated into any other product or transported off site. The commercial product is analyzed for purity using gas chromatography. Analysis indicates no presence of 6-tert-butyl-3-(chloromethyl)-2,4-xylenol at the limit of detection (0.02 % by weight).

No workplace monitoring data are available for 6-tert-butyl-3-(chloromethyl)-2,4-xylenol. However, since this substance is contained within a closed system, and because it has limited volatility, there is very limited potential for workplace exposure.

Robust Summaries and Dossier for CAS No. 23500-79-0

Existing Chemical	:	ID: 23500-79-0
CAS No.	:	23500-79-0
Product name	:	A-1846
EINECS Name	:	6-tert-butyl-3-(chloromethyl-2,4-xylenol
Molecular Formula	:	C13H19ClO

Producer related part

Company	:	Cytec Industries Inc.
Creation date	:	06.05.2003

Substance related part

Company	:	Cytec Industries Inc.
Creation date	:	06.05.2003
Status	:	
Memo	:	
Printing date	:	29.05.2003
Revision date	:	06.05.2003
Date of last update	:	29.05.2003
Number of pages	:	27
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

1.1.1 GENERAL SUBSTANCE INFORMATION

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

2,4-dimethyl-3-(chloromethyl)-6-tert-butylphenol

3-(chloromethyl)-6-(1,1-dimethylethyl)-2,4-dimethylphenol

4-tert-butyl-3-hydroxy-2,6-dimethylbenzyl chloride

6-tert-butyl-2,4-dimethyl-3-chloromethyl phenol

6-tert-butyl-3-chloromethyl-2,4-dimethylphenol

phenol, 3-(chloromethyl)-6-(1,1-dimethylethyl)-2,4-dimethyl-

phenol, 6-tert-butyl-3-chloromethyl-2,4-xylenol

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : industrial
Category : Chemical industry: used in synthesis

Reliability : (1) valid without restriction
11.05.2003

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= 45 °C
Sublimation	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The melting point of 45 degrees C is for the pure crystallized substance. The product is usually isolated with 11-13% methyl isobutyl ketone (CAS No. 108-10-1) added to store and handle the product in liquid form (Cytec Industries, Inc. material safety data sheet dated 10/30/00 for A-1846).
Reliability	:	(2) valid with restrictions Methodology was not documented.
Flag	:	Critical study for SIDS endpoint

11.05.2003 (4)

Value	:	= -32 °C
Sublimation	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS
Test substance	:	The material is the commercially stored form containing 11-13% methyl isobutyl ketone solvent.
Reliability	:	(2) valid with restrictions Experimental details were not provided.

22.05.2003 (3)

2.2 BOILING POINT

Value	:	ca. 320 °C at 1013 hPa
Decomposition	:	
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN Mpbpwin (v1.40) was used to estimate boiling point by the adapted Stein and Brown Method. Inputs to the model were CAS No. 23500-79-0 and the measured melting point (45 degrees C).
Reliability	:	(2) valid with restrictions Data were obtained by modeling.
Flag	:	Critical study for SIDS endpoint

11.05.2003 (10)

Value	:	= 156 °C at
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS
Test substance	:	The material is the commercially stored form containing 11-13% methyl isobutyl ketone solvent.

Reliability : (2) valid with restrictions
Experimental details were not provided.
22.05.2003 (3)

2.3 DENSITY

Type : relative density
Value : ca. 1.044 g/cm³ at 20 °C
Method : other
Year :
GLP : no
Test substance : other TS

Test substance : The material is the commercially stored form containing 11-13% methyl isobutyl ketone solvent.
Reliability : (2) valid with restrictions
Experimental details were not provided.
11.05.2003 (3)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value : ca. .00018 hPa at 25 °C
Decomposition :
Method : other (calculated)
Year : 2003
GLP : no
Test substance : as prescribed by 1.1 - 1.4

Remark : EPIWIN Mpbpwin (v1.40) was used to estimate the vapor pressure by the Modified Grain Method. Inputs to the model are CAS No. 23500-79-0 and the measured melting point (45 degrees C).
Reliability : (2) valid with restrictions
Data were obtained by modeling.
11.05.2003 (10)

Value : ca. 12 hPa at 20 °C
Decomposition :
Method : other (measured)
Year :
GLP : no
Test substance : other TS

Remark : The vapor pressure conforms to that of the solvent.
Test substance : The substance is in liquid form, diluted by 11-13% methyl isobutyl ketone solvent.
Reliability : (2) valid with restrictions
Experimental details were not provided.
14.05.2003 (3)

2.5 PARTITION COEFFICIENT

Partition coefficient	:	octanol-water
Log pow	:	= 5.32 at 20 °C
pH value	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN Kowwin (v1.66) was used to estimate the log Kow (Pow). Inputs to the model are CAS No. 23500-79-0 and the measured melting point (45 degrees C).
Reliability	:	(2) valid with restrictions Data were obtained by modeling.
Flag	:	Critical study for SIDS endpoint

11.05.2003 (9)

Partition coefficient	:	octanol-water
Log pow	:	= 3.9 at °C
pH value	:	
Method	:	other (measured)
Year	:	
GLP	:	no data
Test substance	:	other TS
Test substance	:	The material is the commercially stored form containing 11-13% methyl isobutyl ketone solvent.
Reliability	:	(2) valid with restrictions Experimental details were not provided.

22.05.2003 (3)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	= 10.19 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	slightly soluble (0.1-100 mg/L)
Stable	:	yes
Deg. product	:	
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN Wskow (v1.40) was used to estimate the water solubility. Inputs to the model are CAS No. 23500-79-0 and the measured melting point (45 degrees C).
Reliability	:	(2) valid with restrictions Data were obtained by modeling.

14.05.2003 (11)

Solubility in	:	Organic Solvents
Value	:	at °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	

pKa	:	at 25 °C
Description	:	of very high solubility
Stable	:	yes
Deg. product	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The pure crystalline substance can be liquified and dissolved into one liquid phase by adding 11-13% by weight methyl isobutyl ketone.
Reliability	:	(2) valid with restrictions Experimental details were not provided.

22.05.2003 (3)

Solubility in	:	Water
Value	:	= 500 mg/l at 25 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	other TS
Test substance	:	The material is the commercially stored form containing 11-13% methyl isobutyl ketone solvent.
Reliability	:	(2) valid with restrictions Experimental details were not provided.

22.05.2003 (3)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	Sun light
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	
Rate constant	:	= .0000000000143539 cm³/(molecule*sec)
Degradation	:	= 50 % after 8.9 hour(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN Aop Program (v1.90) was used to calculate the hydroxyl radical rate constant and half life. A CAS No. of 23500-79-0 was inputted.
Reliability	:	(2) valid with restrictions
Flag	:	Critical study for SIDS endpoint

14.05.2003 (6)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Remark	:	EPIWIN Hydrowin(v1.67) cannot estimate a rate constant for molecules other than esters, carbamates, epoxides, halomethanes and specific alkyl halides.

14.05.2003

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	
Air	:	.0002 % (Fugacity Model Level I)
Water	:	11.6 % (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	40.8 % (Fugacity Model Level II/III)
Soil	:	47.6 % (Fugacity Model Level II/III)
Method	:	other

Year	:	2003
Remark	:	Inputs into the EPIWIN Program were a measured melting point of 45 degrees C , a CAS No. of 23500-79-0, and an emission rate to air of 0 kg/hr.
Result	:	Half-lives in various media based on EPIWIN Biowin and EPIWIN aop are air = 17.88 hours, water = 1440 hours, soil =1440 hours, and sediment = 5760 hours. Biowin ultimate is estimated to be months. The EPIWIN Pckoc Program (v1.66) estimates the soil/sediment partition constant to be 1.705 E+4. EPIWIN Henry (v3.10) was used to calculate a Henry's Law Constant of 6.85 E-7 atm-m3/mole at 25 degrees C.
Reliability	:	(2) valid with restrictions Data were obtained by modeling.
Flag	:	Critical study for SIDS endpoint

22.05.2003 (8)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type	:	aerobic
Inoculum	:	
Deg. product	:	
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN Biowin (v4.00) was used to predict biodegradability. A CAS No. of 23500-79-0 was inputted into the model.
Result	:	Linear Model Prediction: biodegrades fast (probability of 0.5694) Non-linear Model Prediction: does not biodegrade fast (probability of 0.1513) Ultimate Biodegradation Timeframe: months (value = 2.2195) Primary Biodegradation Timeframe: weeks (value = 3.1692) MITI Linear Model Prediction: does not biodegrade fast (value = 0.272) MITI Non-Linear Model Prediction: does not biodegrade fast (value = 0.0430)
Reliability	:	(2) valid with restrictions Data were obtained by modeling.

14.05.2003 (12)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Elimination	:	
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark	:	Inputs into the EPIWIN Program were a measured melting point of 45 degrees C, a CAS No. of 23500-79-0, and an emission rate to air of 0 kg/hr.
Result	:	The log bioconcentration factor (log BCF) is calculated [EPIWIN BCF Program (v2.14)] to be 2.945.
Reliability	:	(2) valid with restrictions Data were obtained by modeling.

22.05.2003 (8)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	other
Species	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN ECOSAR (v0.99) was used to obtain the calculated LC50 value. Inputs to the model are CAS Number 23500-79-0 and the measured melting point (45 degrees C).
Result	:	The LC50 values were 0.3 or 0.118 mg/l, depending on whether the molecule was classified as a phenol or benzyl halide (respectively).
Reliability	:	(2) valid with restrictions Data were obtained by modeling.

14.05.2003 (7)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	other
Species	:	Daphnia sp. (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
Analytical monitoring	:	no
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	EPIWIN ECOSAR (v0.99) was used to obtain the calculated LC50 value. Inputs to the model are CAS Number 23500-79-0 and the measured melting point (45 degrees C).
Result	:	The LC50 values were 0.535 or 0.118 mg/l, depending on whether the molecule was classified as a phenol or benzyl halide (respectively).
Reliability	:	(2) valid with restrictions Data were obtained by modeling.

14.05.2003 (7)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	other algae: green
Endpoint	:	
Exposure period	:	96 hour(s)
Unit	:	mg/l
Limit test	:	
Analytical monitoring	:	no
Method	:	other
Year	:	2003
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4

Remark	:	EPIWIN ECOSAR (v0.99) was used to obtain the calculated LC50 value. Inputs to the model are CAS No. 23500-79-0 and the measured melting point (45 degrees C).
Result	:	The LC50 values were 0.13 or 0.118 mg/l, depending on whether the molecule was classified as a phenol or benzyl halide (respectively).
Reliability	:	(2) valid with restrictions Data were obtained by modeling.

14.05.2003 (7)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	= 7.71 ml/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male
Number of animals	:	10
Vehicle	:	
Doses	:	5 and 10 ml/kg
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Based on a specific gravity of 1.044 at 20 degrees C, the LD50 dose in g/kg is 8.04.
Result	:	Four animals treated with 10 ml/kg died; 2 between 6-24 hours of dosing and the others on days 2 or 3 after dosing. None of the animals exposed to 5 ml/kg died. The LD50 value calculated was 7.71 (5.71 to 10.4) ml/kg. All animals had a sluggish, unsteady gait after 1 hour of treatment. All animals treated with 5.0 ml/kg recovered within 2 days. Two animals treated with 10 ml/kg were prostate 1 day after treatment. One of these animals recovered on day 2 (the other died on either day 2 or 3; see above). Survivors gained an average of 75 g over the course of the study. Animals that died exhibited distended, gas-filled and injected stomachs, with glandular portions mottled pink and yellow; red kidney medullae; distended, liquid, blood-filled and injected intestines that were yellow and red in areas; and red adrenals. Survivors exhibited stomachs adhered to abdominal walls and livers at necropsy.
Test condition	:	Two groups of 5 nonfasted, male Hilltop-Wistar rats (90-120 g) were given 5.0 or 10.0 ml/kg test material by the oral route (presumably by gavage) as received. The length of the observation period after dosing is not clear (from 3-14 days); however, it probably was the standard 14 days since animals almost doubled their weight over the course of the experiment. All animals that died were subjected to gross necropsy. It is not clear when animals were terminated (from 3-14 days); however, they were necropsied at that time. The method of calculating the LD50 value was not listed.
Test substance	:	The test material was 80.5% pure. It is assumed that the material was the commercially isolated material that contains 11-13% methyl isobutyl ketone. It also contained 5.5% 6-t-butyl-2,4-dimethyl phenol. Other impurities were not identified.
Reliability	:	(2) valid with restrictions The purity of the test material was not high. It is not known if doses were corrected for purity. The method of calculating the LD50 value was not listed. Only one sex was tested.
Flag	:	Critical study for SIDS endpoint

14.05.2003 (1)

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley

Sex	:	male/female
Number of animals	:	6
Vehicle	:	other: dried arachis oil BP
Doses	:	2000 mg/kg
Method	:	OECD Guide-line 423
Year	:	2000
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result : None of the animals died. Hunched posture and diarrhea were noted after treatment in all animals and lethargy and pilo-erection were found in males. Animals recovered 2-4 days after dosing. All animals gained a normal amount of weight over the observation period. No abnormalities were found at necropsy.

Test condition : The test material was freshly prepared as a suspension at 200 mg/ml in dried arachis oil BP. Homogeneity was assured by used of a Silverson homogenizer and vortex mixer. Animals [Sprague-Dawley Crl: CD(SD)IGSBR] were acclimated for at least 5 days before treatment. At the start of the study the males and females weighed 202 to 226 g and 216 to 230 g, respectively, and were approximately 8 weeks of age.

Animals were allowed free access to food and water with the exception of an overnight fast immediately before dosing and for approximately 3-4 hours after dosing. The diet, drinking water and bedding were routinely analyzed for contaminants that could affect the outcome.

Animals were housed in groups of 3/sex in rooms maintained at 19-25 degrees C, 30-70% relative humidity, and under a 12-hr light/dark cycle.

All animals (3 per sex) were dosed with 2000 mg/kg at a volume of 10 ml/kg by gavage. The volume administered was calculated according to the fasted body weight at the time of dosing (females 216 - 230 g and males 202 - 226 g). Females were dosed prior to males. Sufficient time was allowed between dosing to confirm the survival of previously dosed animals.

The animals were observed for death or overt signs of toxicity 0.5, 1, 2, and 4 hours after dosing and then daily for 14 days. Animals were weighed 7 and 14 days after treatment. Animals were killed by cervical dislocation 14 days after treatment. All animals were subjected to gross necropsies. External and internal (major organs) examinations were conducted. The appearance of any macroscopic abnormalities was recorded. No tissues were retained.

Test substance : The material was described as "purified A-1846". However, the exact purity of the material was not listed. The material was a white solid. According to a MSDS supplied by the manufacturer, unpurified material can contain 11-13% methyl isobutyl ketone. It is assumed that this material was removed during purification, since it is a liquid.

Reliability : (2) valid with restrictions
Only one dose was tested. The purity of the material is unknown.

07.05.2003 (5)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 2000 ppm
Species	:	rat
Strain	:	
Sex	:	
Number of animals	:	6

Vehicle	:	
Doses	:	
Exposure time	:	4 hour(s)
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	All 6 rats survived a 4-hour exposure to 2000 ppm (8.36 mg/l).
Reliability	:	(4) not assignable There are not enough details to assign a reliability rating.

07.05.2003 (3)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	= 9.98 ml/kg bw
Species	:	rabbit
Strain	:	New Zealand white
Sex	:	male
Number of animals	:	14
Vehicle	:	
Doses	:	0.8, 3.2, 6.4, 10.0 ml/kg
Method	:	other
Year	:	1979
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Based on a specific gravity of 1.044 at 20 degrees C, the LD50 dose in g/kg is 10.4.
Result	:	One animal treated with 3.2 ml/kg died on day 3. Two animals treated with 10.0 ml/kg died (one on day 3 and another on day 5). The LD50 value was 9.98 (4.41 to 22.6) ml/kg. No clinical signs of systemic toxicity were noted. Surviving animals in all groups treated with 3.2 to 10 ml/kg lost weight over the course of the study. Erythema, edema and ecchymosis and areas of necrosis were noted at the test site in several animals over the course of the study (times at which these observations were recorded were not noted). Scabs were noted in an undetermined number of animals at 14 days. Gross necropsies of survivors were normal. The animals that died exhibited red kidneys.
Test condition	:	Skin of the 14 animals (avg wt. 2246 - 2543 mg/kg) was clipped prior to treatment. Undiluted test material was applied at 0.8 ml/kg to two rabbits and at 3.2, 6.4 and 10.0 ml/kg to 3 groups of 4 animals each. The application site was then covered for 24 hours. Animals were observed for 14 days and weighed prior to euthanization and necropsy. Animals that died also were subjected to necropsy.
Test substance	:	The test material was 80.5% pure. It is assumed that the material was the commercially isolated material that contains 11-13% methyl isobutyl ketone. It also contained 5.5% 6-t-butyl-2,4-dimethyl phenol. Other impurities were not identified.
Reliability	:	(2) valid with restrictions The purity of the test material was not high. It is not known if doses were corrected for purity. The method of calculating the LD50 value was not listed. Only one sex was tested.

14.05.2003 (1)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	Semiocclusive
Exposure time	:	
Number of animals	:	6
Vehicle	:	
PDII	:	7
Result	:	highly irritating
Classification	:	
Method	:	Draize Test
Year	:	1979
GLP	:	no data
Test substance	:	other TS
Result	:	The mean values for erythema at intact sites were 2.17 and 4.00 after 24 or 72 hours, respectively. For abraded sites, these scores were 2.50 and 4.00, respectively. The mean values for edema at intact sites were 3.50 and 4.00 after 24 or 72 hours, respectively. At abraded sites, these scores were 3.83 and 4.00, respectively. The primary irritation score was 7.00. The structure of the tissue at the site of contact was destroyed or changed irreversibly in 24 hours or less.
Test condition	:	Test material (0.5 ml) was applied under a covered patch to both intact and abraded sites (the number of sites was not stated). The contact time was not stated. Skin was evaluated 24, and 72 hours after application for erythema and edema. The study was conducted according to an "FHSA procedure" and reactions were scored according to the method of Draize et al., J Pharmacol Exper Ther 82:377, 1944. The maximum possible value for a skin reaction (excluding necrosis) was 4. The primary irritation score was the sum of the mean values divided by 4.
Test substance	:	The test material was 80.5% pure. It is assumed that the material was the commercially isolated material that contains 11-13% methyl isobutyl ketone. It also contained 5.5% 6-t-butyl-2,4-dimethyl phenol. Other impurities were not identified.
Reliability	:	(1) valid without restriction The study was conducted according to an established method.

14.05.2003 (1)

Species	:	rabbit
Concentration	:	undiluted
Exposure	:	no data
Exposure time	:	4 hour(s)
Number of animals	:	6
Vehicle	:	
PDII	:	
Result	:	
Classification	:	
Method	:	other: DOT test
Year	:	1980
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Result	:	None of the 6 animals had necrosis. Therefore, the test material was not corrosive. No irritation scores were given.
Test substance	:	The test material was 80.5% pure. It also contained 5.5% 6-t-butyl-2,4-dimethyl phenol. Other impurities were not identified.

Reliability	:	(4) not assignable There are not enough details to assign a reliability rating.

14.05.2003 (13)

5.2.2 EYE IRRITATION

Species	:	rabbit
Concentration	:	undiluted
Dose	:	.1 ml
Exposure time	:	
Comment	:	
Number of animals	:	6
Vehicle	:	
Result	:	highly irritating
Classification	:	irritating
Method	:	Draize Test
Year	:	1979
GLP	:	no data
Test substance	:	other TS

Result	:	The average corneal, iridial and conjunctival scores at 24 hours were 28.3, 4.2 and 13.7, respectively. At 48 hours, these values were 21.7, 4.2 and 13.3, respectively. At 72 hours, they were 18.3, 0.8 and 11.7, respectively. At any of the readings made at 24, 48 and 72 hours there was: 1) discernable opacity or ulceration of the cornea other than a slight dulling of the normal luster, 2) inflammation of the iris other than slight deepening of the folds, or slight circumcorneal injection, 3) a diffuse, deep-crimson red appearance of the conjunctivae, with individual vessels not easily discernable, and 4) an obvious swelling of the conjunctivae excluding cornea and iris, with partial eversion of the lids. There also was tissue destruction or irreversible change of tissue in 24 hours or less.
Test condition	:	Test material (0.1 ml) was applied to eyes of 6 rabbits. Eyes were evaluated 24, 48 and 72 hours later. They do not appear to have been washed. The test was conducted according to an "FHSA procedure" and eyes were scored according to the method of Draize et al. (J Pharmacol Exper Ther 82:377, 1944). The maximum possible scores for eye irritation reactions (excluding necrosis) are cornea: 80; iris: 10; and conjunctivae:20.
Test substance	:	It is assumed that the material was the commercially isolated material that contains 11-13% methyl isobutyl ketone.
Reliability	:	(1) valid without restriction The study was conducted according to an established method.

14.05.2003 (1)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	S. typhimurium strains TA98, TA100, TA1535 and TA1537 and E. Coli WP2uvrA-
Test concentration	:	5 to 1500 micrograms/plate for Salmonella strains; 50 to 5000 micrograms/plate for E. coli

Cytotoxic concentr.	:	500 micrograms/plate (without S-9) and 1500 micrograms/plate (with S-9) for Salmonella strains; 5000 micrograms/plate for E. coli
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	2000
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Result : The preliminary experiment revealed that the test material was toxic at concentrations > = 500 and 1500 micrograms/plate in strain TA100 without and with S-9, respectively. Although the background lawn was reduced somewhat in WP2uvrA- exposed to 5000 micrograms/plate (without S-9), toxicity was not considered to be excessive. Therefore, 1500 and 5000 micrograms/plate were the upper limits of concentrations in the mutation study with Salmonella and E. coli, respectively.

In both experiments, there was no significant increase in the number of mutants in any strains incubated with any concentration of test material (with or without S-9). All of the positive controls induced at least a 3-fold increase in the number of revertants. No precipitate was observed on the plates in the presence or absence of S-9. Spontaneous mutation rates in negative controls were acceptable.

Test condition : The Salmonella strains were obtained from the University of California at Berkeley, and E coli strain WP2uvrA- was obtained from the British Biological Research Association. Bacteria were stored frozen until used. Prior to use, characterization checks were carried out to confirm the amino-acid requirement, presence of rfa, R factors, uvrA or uvrB mutation and the spontaneous reversion rate. Overnight sub-cultures were prepared in nutrient broth and incubated at 37 degrees C for approximately 10 hours. Each culture was monitored spectrophotometrically for turbidity with titres determined by viable count analysis on nutrient agar plates.

The test material was weighed and approximate half-log dilutions prepared in dried dimethyl sulfoxide. A preliminary study using 0.15 to 5000 micrograms/plate was used to determine the toxicity of the material. Based on the results, the mutation study with the 4 Salmonella strains was conducted with 5, 15, 50, 150, 500, and 1500 micrograms/plate, and the study with E. coli was performed with 50, 150, 500, 1500 and 5000 micrograms/plate.

Measured aliquots (0.1 ml) of each of the bacterial cultures were dispensed into sets of test tubes followed by 2.0 ml of molten, trace histidine supplemented top agar, 0.1 ml of the test material formulation, vehicle or positive control [2, 3 or 5 micrograms/plate N-ethyl-N'-nitro-N-nitirosoguanidine (ENNG) for E. coli WP2uvrA- and Salmonella strains TA100 and TA1535 without S-9, respectively; 80 micrograms/plate 9-aminoacridine (AA) for strain TA1537 without S-9; 0.2 micrograms/plate 4-nitroquinoline-1-oxide (4NQO) for strain TA98 without S-9; 1 or 10 micrograms/plate 2-aminoanthracene (2AA) for Salmonella strain TA100 and E. coli WP2uvrA- with S-9, respectively; 2 micrograms/plate 2AA for strains TA1535 and TA1537 with S-9; and 5 micrograms/plate benzo(a)pyrene (BP) for strain TA98 with S9], and either 0.5 ml S9-mix or phosphate buffer. S-9 was prepared in-house from the livers of male Sprague-Dawley rats that had been orally induced with phenobarbitone/ beta-naphthoflavone. The contents of each test tube were mixed and equally distributed onto the surface of Vogel-Bonner Minimal agar plates (one tube per plate). The procedure was repeated in triplicate, for each bacterial strain and for each concentration of test material (with and without S-9 mix).

All plates were incubated at 37 degrees for approximately 48 hours and the

frequency of revertant colonies assessed using a Domino colony counter.

A second experiment was performed using the same test conditions as in the first.

An experiment was considered valid if all vehicle and untreated controls had numbers of spontaneous revertants within historical ranges, the appropriate characteristics of each tester strain were confirmed, all tester strain cultures had approximately 1 to 9.9 x 10E9 bacteria/ml before treatment, positive controls induced at least a 2-fold increase in revertants, there was a minimum of 4 non-toxic test material doses, and there was no evidence of excessive contamination.

A test material was considered positive in the assay if the material induced a reproducible, dose-related and statistically (Dunnett's method of linear regression) significant increase in revertants in at least one strain.

Test substance : The material was described as "purified A-1846". However, the exact purity of the material was not listed. The material was a white solid. According to a MSDS supplied by the manufacturer, unpurified material can contain 11-13% methyl isobutyl ketone. It is assumed that most of this material was removed during purification.

Reliability : (2) valid with restrictions
Purity of the test material was not listed.

Flag : Critical study for SIDS endpoint

07.05.2003 (14)

Type : Ames test
System of testing : S. typhimurium strains TA-98, TA-100, TA-1535, and TA-1537 and E. coli strain WP2uvrA-
Test concentration : 1000 micrograms/plate
Cytotoxic concentr. : 1000 micrograms/plate
Metabolic activation : with and without
Result : negative
Method : other
Year : 1978
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Result : The results of the tests were negative. Large zones of inhibition were present on all plates in the disc test.

Test condition : Test material was dissolved in ethanol. A disc test was performed on all strains and a plate test was performed on strains TA-1535 and TA-1537. The material was tested with and without metabolic activation. Only one dose was tested (1000 mg/plate or disc). No other study details were given.

Test substance : Purity of the test material was 90.1%. Impurities were not listed. The concentration tested was based on 100% active material.

Reliability : (4) not assignable
There are not enough details to assign a reliability rating.

07.05.2003 (2)

5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) Brown DR. 1979. Antioxidant A-1846 Range Finding Toxicity Tests: Single Oral Dose, Single Dermal Dose, Skin Irritation, Eye Irritation. Carnegie-Mellon University Institute of Research, Report No 42-556, for American Cyanamid Company, dated July 26.

(2) Caterson C. 1978. Mutagenicity test report (Ames Salmonella test) for A-1846. Report Number M78-170 from CRD Division, Plastics Additives Department (Company ????)

(3) Cytec Industries, Inc. 2000. Material safety data sheet for A-1846, dated 10/30/2000. .

(4) Cytec Industries, Inc. 2003. Communication.

(5) Driscoll R. 2000. Purified A-1846 (CT-684-00). Acute oral toxicity in the rat - acute toxic class method. SafePharm Laboratories Limited Project Number 971/115 for Cytec Industries Inc., dated October 3.

(6) EPIWIN Aop Program (v1.90).

(7) EPIWIN ECOSAR (v0.99).

(8) EPIWIN Fugacity Level III Program

(9) EPIWIN Kowwin (v1.66).

(10) EPIWIN Mpbpwin (v1.40).

(11) EPIWIN Wskow (v1.40).

(12) EPIWRSIN Biowin (v4.00).

(13) Shaffer CB. 1980. Antioxidant A-1846 skin irritation test (D.O.T.). Carnegie-Mellon University Institute of Research Report No. 43-502 to American Cyanamid Company, dated January 31.

(14) Thompson PW. 2000. Purified A-1846 (CT-684-00). Reverse mutation assay "Ames Test" using Salmonella Typhimurium and Escherichia Coli. SafePharm Laboratories Limited Project Number 971/116 for Cytec Industries Inc., dated October 30.

10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT